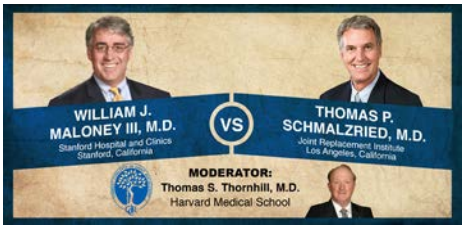
VOLUME 9, ISSUE 5 | FEBRUARY 12, 2013

# Orthopedics This Week

## week in review









## breaking news



**For all news that is ortho, read on**

# Orthopedic Power Rankings

## Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

**THIS WEEK:** Clearly orthopedic stocks are in favor with investors "discovering" these solid, cash flow rich medical device firms. Compared with other sectors in healthcare, orthopedic companies are probably the best performers. Why? Strong core demand for products. Excellent cash flows. Growing demand among the billion aging patients in China and India.

| RANK | LAST WEEK | COMPANY | TTM OP MARGIN | 30-DAY PRICE CHANGE | COMMENT |
|---|---|---|---|---|---|
| 1 | 2 | Globus Medical | 29.39% | 20.82% | After an initial dip, investors are figuring out what an extraordinary combination of profits and growth GMED is. |
| 2 | 1 | Stryker | 23.68 | 9.25 | "Back on Track" is how institutional investors are characterizing SYK under the new management team. |
| 3 | 6 | Exactech | 8.64 | 10.61 | Buyers are soaking up EXAC—which is interesting. Solid $230 million ortho manufacturer at very attractive valuations. |
| 4 | 5 | Medtronic | 28.65 | 8.58 | The key here is that market share may well have stabilized due to a steady stream of new products and innovation. |
| 5 | 4 | Zimmer | 25.45 | 7.48 | The key to ZMH is that 25% of every sales dollar is profit and that puts current valuations at very low P/E levels. |
| 6 | 3 | NuVasive | 7.08 | (2.69) | After a nice run NUVA seems ready for a near term pull back. Longer term, NUVA's superior management will prove out over time. |
| 7 | 7 | Integra LifeSciences | 13.73 | 4.85 | IART's valuations remain comparatively low. To move up, company needs a sales growth catalyst. |
| 8 | 9 | Johnson & Johnson | 25.58 | 5.23 | The #1 question is how much impact will MOM litigation will have on future implant sales. Not much, we think. |
| 9 | 8 | Symmetry Medical | 5.63 | (0.09) | SMA is a bargain, but with these low profit margins, the market seems comfortable with such a low PSR. |
| 10 | NR | Conmed | 10.51 | 4.23 | Back on the Power Rankings, this low priced ortho company is now generating double-digit profit margins. |

# Robin Young's Orthopedic Universe

## TOP PERFORMERS LAST 30 DAYS

| | COMPANY | SYMBOL | PRICE | MKT CAP | 30-DAY CHG |
|---|---|---|---|---|---|
| 1 | Globus Medical | GMED | $13.58 | $1,238 | 20.82% |
| 2 | Exactech | EXAC | $18.66 | $248 | 10.61% |
| 3 | Stryker | SYK | $63.78 | $24,249 | 9.25% |
| 4 | Medtronic | MDT | $47.10 | $47,635 | 8.58% |
| 5 | Zimmer Holdings | ZMH | $75.85 | $13,160 | 7.48% |
| 6 | Johnson & Johnson | JNJ | $75.48 | $209,175 | 5.23% |
| 7 | Integra LifeSciences | IART | $42.17 | $1,141 | 4.85% |
| 8 | Conmed | CNMD | $29.60 | $843 | 4.23% |
| 9 | Orthofix | OFIX | $38.40 | $742 | 3.98% |
| 10 | MiMedx Group | MDXG | $4.35 | $377 | 3.82% |

## WORST PERFORMERS LAST 30 DAYS

| | COMPANY | SYMBOL | PRICE | MKT CAP | 30-DAY CHG |
|---|---|---|---|---|---|
| 1 | Alphatec Holdings | ATEC | $1.56 | $142 | -12.36% |
| 2 | Bacterin Intl Holdings | BONE | $1.24 | $53 | -7.46% |
| 3 | CryoLife | CRY | $6.21 | $170 | -7.04% |
| 4 | TranS1 | TSON | $2.30 | $63 | -6.12% |
| 5 | TiGenix | TIG.BR | $1.19 | $119 | -5.26% |
| 6 | MAKO Surgical | MAKO | $11.06 | $508 | -4.82% |
| 7 | NuVasive | NUVA | $16.99 | $740 | -2.69% |
| 8 | RTI Biologics Inc | RTIX | $4.03 | $226 | -2.42% |
| 9 | ArthroCare | ARTC | $36.20 | $1,009 | -0.19% |
| 10 | Symmetry Medical | SMA | $10.59 | $390 | -0.09% |

## LOWEST PRICE / EARNINGS RATIO (TTM)

| | COMPANY | SYMBOL | PRICE | MKT CAP | P/E |
|---|---|---|---|---|---|
| 1 | Orthofix | OFIX | $38.40 | $742 | 12.76 |
| 2 | Medtronic | MDT | $47.10 | $47,635 | 13.81 |
| 3 | Smith & Nephew | SNN | $56.25 | $10,179 | 13.96 |
| 4 | Zimmer Holdings | ZMH | $75.85 | $13,160 | 14.26 |
| 5 | Johnson & Johnson | JNJ | $75.48 | $209,175 | 14.77 |

## HIGHEST PRICE / EARNINGS RATIO (TTM)

| | COMPANY | SYMBOL | PRICE | MKT CAP | P/E |
|---|---|---|---|---|---|
| 1 | Wright Medical | WMGI | $22.14 | $878 | 69.19 |
| 2 | NuVasive | NUVA | $16.99 | $740 | 60.68 |
| 3 | Symmetry Medical | SMA | $10.59 | $390 | 46.04 |
| 4 | CryoLife | CRY | $6.21 | $170 | 22.18 |
| 5 | Exactech | EXAC | $18.66 | $248 | 21.95 |

## LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

| | COMPANY | SYMBOL | PRICE | MKT CAP | PEG |
|---|---|---|---|---|---|
| 1 | Orthofix | OFIX | $38.40 | $742 | 1.11 |
| 2 | RTI Biologics Inc | RTIX | $4.03 | $226 | 1.28 |
| 3 | Conmed | CNMD | $29.60 | $843 | 1.37 |
| 4 | Globus Medical | GMED | $13.58 | $1,238 | 1.43 |
| 5 | Zimmer Holdings | ZMH | $75.85 | $13,160 | 1.48 |

## HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

| | COMPANY | SYMBOL | PRICE | MKT CAP | PEG |
|---|---|---|---|---|---|
| 1 | Wright Medical | WMGI | $22.14 | $878 | 7.54 |
| 2 | NuVasive | NUVA | $16.99 | $740 | 5.91 |
| 3 | CryoLife | CRY | $6.21 | $170 | 5.54 |
| 4 | Symmetry Medical | SMA | $10.59 | $390 | 3.84 |
| 5 | Smith & Nephew | SNN | $56.25 | $10,179 | 2.31 |

## LOWEST PRICE TO SALES RATIO (TTM)

| | COMPANY | SYMBOL | PRICE | MKT CAP | PSR |
|---|---|---|---|---|---|
| 1 | Alphatec Holdings | ATEC | $1.56 | $142 | 0.72 |
| 2 | Symmetry Medical | SMA | $10.59 | $390 | 1.09 |
| 3 | Conmed | CNMD | $29.60 | $843 | 1.16 |
| 4 | Exactech | EXAC | $18.66 | $248 | 1.21 |
| 5 | RTI Biologics Inc | RTIX | $4.03 | $226 | 1.27 |

## HIGHEST PRICE TO SALES RATIO (TTM)

| | COMPANY | SYMBOL | PRICE | MKT CAP | PSR |
|---|---|---|---|---|---|
| 1 | TiGenix | TIG.BR | $1.19 | $119 | 104.02 |
| 2 | MiMedx Group | MDXG | $4.35 | $377 | 48.62 |
| 3 | MAKO Surgical | MAKO | $11.06 | $508 | 6.01 |
| 4 | Globus Medical | GMED | $13.58 | $1,238 | 3.73 |
| 5 | TranS1 | TSON | $2.30 | $63 | 3.28 |

*PSR: Aggregate current market capitalization divided by aggregate sales and the calculation excluded the companies for which sales figures are not available.*

# Laser Spine Institute on Trial

By Walter Eisner

Airline travelers have seen the magazine ad showing two topless women in bikini bottoms, their backs to the viewer. One of them wears a Band-Aid. "Who just had back surgery?" a caption asks.

The ad promotes the laser surgical procedures performed at the Laser Spine Institute LLC (LSI).

## "Largest Spine Center in the World"

According to a May 2011 story written by David Armstrong of *Bloomberg News*, as many as 5,000 procedures are performed annually at LSI surgical centers in Phoenix, Philadelphia, Oklahoma City and Tampa. The company bills itself as the "largest spine center in the world," with sales in 2010 of $109 million. That's about $21,800 per procedure according to our math.

While the overall spine surgery revenues have been under severe pressure, (Wall Street analysts estimate that spinal implant supplier revenues declined 0.4% in 2012 and the number of fusion procedures following diagnosis of degenerative disc disease has been declining steadily for the past three years) due to a much tougher reimbursement environment which is characterized by a rising tide of insurance coverage denials insurance carriers, LSI seems to be immune from the headwinds faced by every other spine care provider.

LSI's sales and procedure volumes seem to be flying way above the rest of the spine care industry. Indeed, LSI booked

*Wikimedia Commons and SSGT Tia Schroeder, USAF/Andrew Huth/RRY Publications LLC*

*Wikimedia Commons and U.S. Navy photo by Photographer's Mate Airman Apprentice Leah Gaines*

a remarkably high 34.3% net profit margin from 2006 through 2009.

According to patient interviews conducted by *Bloomberg*'s Armstrong and copies of billing records he reviewed, LSI often charges $30,000 for each procedure. That's twice as much as Aetna Inc., the third largest U.S. health insurer, will pay for laser-less surgery. According to the corporate controller at Westchester, Illinois-based Regent Surgical health—which operates 15 outpatient centers—it's more than twice the average reimbursement for spine procedures.

From 2006 through 2009, according to recently obtained court documents, LSI earned net income of $98.9 million on revenue of $288 million. Of that amount, $77 million, according to Armstrong, has gone to a small group of shareholders. James St. Louis, D.O., the company founder, purportedly received 25% of that. LSI disputes that figure. Other investors include a Dallas investment firm and two Outback Steakhouse founders.

In 2009 when the company considered an initial public offering, Goldman

Sachs valued the LSI at around $428 million.

## The Hulk Brings Scrutiny

Things appeared to be sailing along, until Terry Bollea, (aka Hulk Hogan) filed a $50 million lawsuit against LSI and, in the process, attracted the glare of the national spotlight on the privately held but, through their new ubiquitous ads, well known company. The complaint opened a window on this secretive company and the particular form of treatment for spine disease performed at LSI. Most ominous for LSI, the lawsuit examined promised patient outcomes against results—with Hulk Hogan acting as spokesperson for unhappy patients.

## Ablation and Decompression

About 80% of Laser Spine's patients get the same two-step procedure, according to Robert Gruber, a physician who directs spinal diagnostics at the LSI center in Tampa. First the surgeon burns off (ablates) sensitive nerve endings in the joints between vertebrae. Then, he removes herniated disc material or bone spurs that press on nerves and cause pain. In short, said Gruber, the LSI physicians decompress the nerves and perform a laminotomy.

The evidence that ablation—the laser-assisted process that gives the institute its name—helps patients is "pretty weak," Roger Chou, a physician at the Oregon Health & Science University in Portland who is the director of the American Pain Society's clinical guidelines program, told *Bloomberg News*.

"Even in studies showing some benefit, the benefit is small and doesn't last that long," Chou said. "Nerve endings can regenerate over time."

Decompression is generally successful in treating 60 to 70% of patients with spinal stenosis says Jon Lurie, a spine doctor and researcher at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire.

"Spinal stenosis is our bread and butter," said LSI's Gruber said in the *Bloomberg* article. Still, unaffiliated surgeons have treated former Laser Spine patients who didn't need the procedure and shouldn't have gotten it, said Choll W. Kim, a San Diego surgeon who founded the Society for Minimally Invasive Spine Surgery.

Kim said LSI's marketing is so powerful but that he and many of his colleagues have seen patients that needed something different and got the laser spine surgery.

## The Hulk's Unstable Back

Bollea claims in his lawsuit that he went to three different spine surgeons in Tampa before going to LSI. He first saw a board certified orthopedic surgeon

who recommended a laminectomy and fusion. A week later he went to the University of South Florida (USF) where he was told that he needed open lumbar fusion. A third surgeon told him he needed an anterior inter-body fusion with instrumentation.

He agreed to schedule and proceed with the surgery at USF.

Before the surgery, Bollea stopped in at LSI to consult with St. Louis. Bollea claims St. Louis told him he didn't need a fusion, that he could fix him and that he would be back to normal wrestling activities "quickly" after LSI treatments. Bollea cancelled his scheduled surgery and agreed to get treatment at LSI.

Bollea now claims that St. Louis should have known that LSI procedures (ablations, rhizotomy, foraminotomy, laminotomy, facetectomy and percutaneous discectomy) would be ineffective for his diagnosed condition.

## LSI Procedures

Over the next 19 months, LSI performed the following procedures on Bollea:

- Feb 28, 2009 – "Destruction By Thermal Ablation Bilateral Sacroiliac Joint Nerves and Paravertebral Facet Joint Nerves Bilateral L2/3, Bilateral L3/4, Right L4/5, and Bilateral L5/S1." Also performed was a "Lumbar Laminotomy (Hemilamniectomy) with Foraminotomy, Including Partial Facetectomy With Decompression of the Nerve Roots Left L4/5."

  After two to three weeks, the pain returned.

- May 21, 2009 – "Destruction By Thermal Ablation Paravertebral Facet Joint Nerves Left L2/3" and a "Lumbar Laminotomy (Hemilamniectomy) with Foraminotomy, Including Partial Facetectomy With Decompression of the Nerve Roots Left L3/4 with Percutaneous Lysis of Adhesion."

  More temporary relief and returning pain.

- October 12, 2009 - "Endoscopic Surgical Rhizotomies of the Facet Joints with Posterior Capsalectomy and Facet Joint Arthroplasty at Right L4/5 and Bilateral L5/S1.

  No relief.

- May 27, 2010 – "Percutaneous Discectomy, L3/4"

  No relief

- June 30, 2010 – "Percutaneous Discectomy, L4/5"

- August 12, 2010 –"Percutaneous Discectomy, L2/3"

## Fusion, Posterior Instrumentation and Scoliosis Correction

On December 20, 2010, Bollea went back to USF and had an anterior lumbar inter-body fusion (L2-L3, L3-L4, and L4-L5) with posterior instrumentation and scoliosis correction. He claims he got significant relief and was able to return to his professional activities in about three months.

Bollea claims his eventual recovery was delayed and that cost him $50 million dollars of income he could otherwise have earned.

## Informed Consent

Did LSI properly inform Bollea and receive informed consent?

*Tony Yeung, M.D.*

We asked Tony Yeung, M.D. about the procedures used on Bollea. Dr. Yeung did not review Bollea's medical records and did not speak to any physicians at LSI. He has seen patients who had previous experience with the LSI center in Phoenix.

## In Defense of Laser Procedures

Yeung told us laser procedures can relieve facet mediated back pain with facet denervation. Symptoms from mild central stenosis and medial facet stenosis can be relieved by laminotomy/laminectomy and removal of the ligamentum flavum. The result can be as good as open fusions without "burning bridges" for a fusion procedure later if the initial relief worsens due to the progression of the degenerative process, usually years later. "Most patients, if fully informed, understand that returning pain can be the result from an aging spine," said Yeung

"Most patients can tolerate a partial deterioration of the initial good result. It's a matter of informed consent based on past experience, honestly explained," continued Yeung.

Bollea claims LSI purports to provide long lasting and permanent remedies

for scoliosis, spondylolisthesis and decreased disc space. For severe conditions, Yeung recommends either non-surgical treatment of decompression and fusion with traditional techniques.

Yeung says he doesn't disagree with the surgeons who advise traditional fusion for these conditions, but has had many patients who reject fusion and get good results with MIS decompression (foraminal decompression) and dorsal ramus (or its branches) visualized ablation for axial back pain.

"I also have patients who rejected their spine surgeon's recommendations, and elect to try an alternative to fusion with good results. About two-thirds of those patients receive good results that allow enough pain relief over two to five years that they are able to avoid fusion. These painful degenerative conditions can be relieved to the patient's satisfaction with MIS decompression and dorsal ramus ablation, but this is with foraminal decompression that does not destabilize the spine." He emphasizes that his technique is not the same as that performed by LSI.

Yeung recommends transforaminal epiduralgrams and therapeutic injections to be performed first, and only those patients with good results from the diagnostic and therapeutic injections would be considered for foraminal decompression and dorsal ramus ablation.

"I would not have repeated the rhizotomies more than once as the second time is not as effective and I have never done it three times," says Yeung.

"If Bollea's allegations are true then there may have been a lack of proper informed consent," added Yeung.

### Throwing the Laser Baby Out With the Bathwater

As a pioneer in the field of minimally invasive spine surgery, Yeung is aware that not every physician is expert at the procedures he has helped develop and not everyone gets the same results he gets. He wants to be careful that we don't throw the baby (MIS) out with the bathwater if ineffective or badly executed procedures are performed on patients.

Bollea is also suing LSI for using his image without his permission. We found the North American Spine Society (NASS) logo on LSI's website. Apparently they used that image without permission because the logo was removed after we asked NASS about it. A NASS spokesperson said LSI did not have permission to use the logo. The *Becker's Orthopedic & Spine* logo is also on their site. We asked Becker's if they have a relationship with LSI. We did not hear back from them.

The Hulkster's lawsuit is bringing the bright light of scrutiny on privately held LSI's financial success. A jury will decide on the financial damages. Public opinion and payers will decide on the veracity of LSI's claims and decide if the baby gets thrown out with the bathwater. ♦

# Gold Injections for Anti-Inflammation?

By Robin Young

*Wikimedia Commons and Andrew Magill as modified by OTW*

From 1935 to the mid-1980s gold in an injectable form was treatment of choice for severe joint pain. Then new anti-inflammatory compounds in the 1980s combined with a dispute between the FDA and Schering Plough in 1998 over production of medical grade gold virtually eliminated gold as an anti-inflammatory treatment in the United States.

In the roughly 50 years that injectable gold was used to treat arthritic patients, scientists were able to document that gold has anti-inflammatory activity, inhibits inflammatory enzymes and affects mitochondrial activity. Specifically, drugs that are gold based inhibit expression of NF kapaB, tumor necrosis factor (TNF) and other cytokines.

A new company, Arthrogen GmbH of Heidelberg, Germany, has developed a novel approach to using gold as an anti-inflammatory.

Founded in 2000 by Professor Ulrich Schneider M.D., Arthrogen has introduced the first new gold based product in decades called GOLDIC (which refers to gold-induced cytokines). This month Arthrogen announced completion of an 8 patient pilot study which came after an even more ambitious 34 patient knee study.

In the most recent study eight patients suffering from lumbar spine disc herniation pain received a series of four gold injections in the region of their affected nerve roots. The injections were given at 3 to 7 day intervals. After one month, according to Dr. Schneider and Arthrogen, patients reported significant pain relief (visual analog scale and global assessment). Again, according to the company, by the fourth injection of GOLDIC some of the patients were virtually symptom free.

Arthrogen describes GOLDIC as a platform technology where the patient's own blood is mixed with gold particles and when injected may trigger increased production of certain cytokines and important proteins like gelsolin. The company is targeting GOLDIC for orthopedic and trauma surgery.

In the firm's first human clinical study of its novel gold injection system, 34

patients with knee osteoarthritis (Kellgren stage 3-4) received four intra-articular injections with GOLDIC. The clinical result was measured by the Knee injury and Osteoarthritis Outcome Score (KOOS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 1, 3, 6, and 12 months post-treatment.

Patients consistently showed significant improvement as the following charts illustrate. *(Below)*

The analysis of the KOOS data showed not only a reduction of symptoms, but also a significant increase of sports activity three months after the GOLDIC treatment.

## A Short History of Injectable Gold

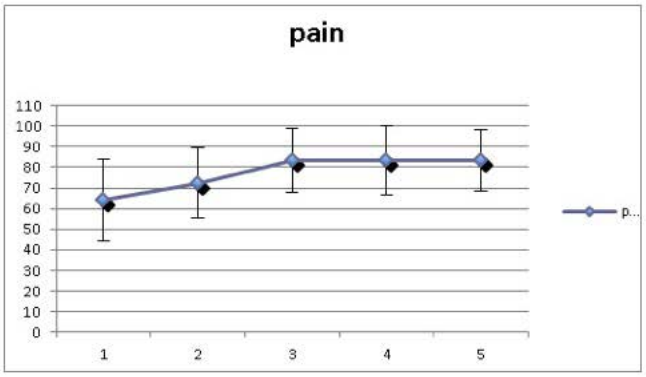
In 1935, Paris-based Jacques Forestier, M.D., published six years of his clinical experience treating 550 patients with gold injections for rheumatoid arthritis, tuberculosis arthritis and ankylosing spondylitis. He reported that a particular form of gold was an effective treatment for these diseases of the musculoskeletal system. (Forestier J. (1935). "Rheumatoid arthritis and its treatment with gold salts—results of six years experience." J Lab Clin Med 20: 827–40.)

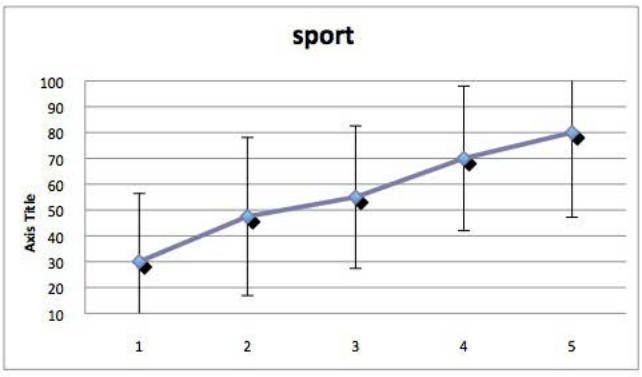
In his landmark retrospective patient survey, Forestier reported that 70% to 80% of his arthritic patients treated with gold salts (more about the specific chemical composition of these "salts" later) responded well to the therapy. In 1936, nine years after he first introduced gold therapy to his European colleagues for arthritis treatment, he expanded his previous review and reported that in chronic progressive rheumatoid polyarthritis patients, the advance of the disease was arrested by gold therapy in 85% of his cases.

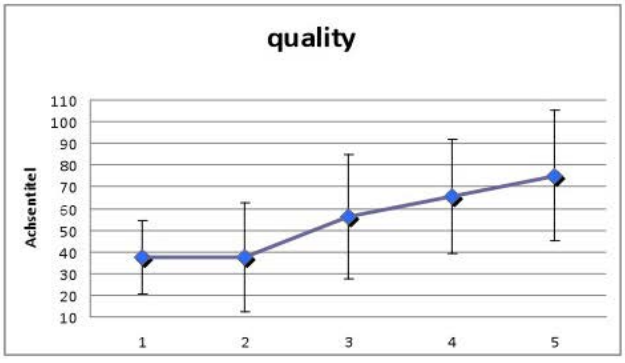
In 1937, Hartfall and Garland reviewed 900 cases of chronic arthritis treated with gold salts over a period of five years. At the time, this was the largest series of cases reported. The two investigators reported clinical improvement in approximately 80% of the cases of rheumatoid arthritis and clinical improvement in approximately 50% of the cases of osteoarthritis. Hartfall and Garland also reported that the benefits of gold salts for osteoarthritis patients were not comparable nor as positive as those for patients with rheumatoid arthritis.

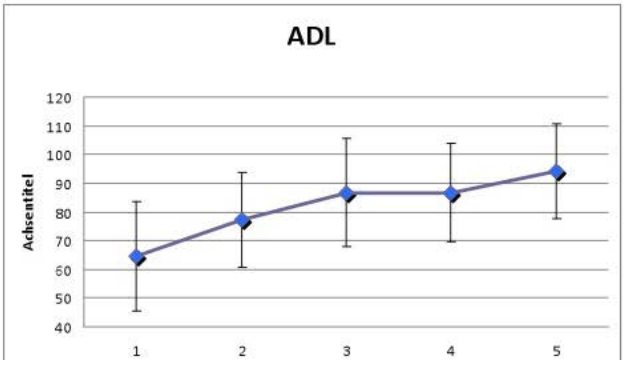
Then in 1961, the British Empire Rheumatism Council sponsored a carefully constructed prospective, double blind, controlled study of the efficacy and toxicity of gold salt treatment for RA. The study, which was published in the *Annals of Rheumatoid Diseases*, showed that patients subjectively experienced improved disease activity, better grip strength, reduced numbers of use of analgesic tablets, lower inflammatory markers and hemoglobin. (a PDF of the study is available at this website: http://ard.bmj.com/content/19/2/95.full.pdf)

From the study: *"On comparing the gold-treated and control groups, it is*




*Arthrogen GmbH*

*apparent that by all criteria, except radiological progression, the gold-treated group showed a definite and greater degree of improvement than the control group from the third month onwards, and this was maintained until the eighteenth month, that is, over one year after completion of the course of injections, although slightly reduced in degree after the twelfth month. A later assessment will be made after a further one year's follow-up, but to date the advantage clearly lies with the gold-treated group. Although part or all of this improvement may disappear within the next few years, one cannot ignore any form of therapy which gives temporary amelioration of symptoms in a progressive and painful disease, unless the hazards of therapy outweigh the advantages: such hardly seems to have been the case in this trial, though skin reactions were troublesome in a significant number of gold-treated patients and albuminuria was noted on four occasions. Steroid therapy and dimercaprol (B.A.L.), not available to the earlier workers with gold salts, can effectively reduce the severity of such side-effects and lessen the dangers of this form of therapy."*

## So, How Does Gold Work?

To start with, the term gold salts is a misnomer. It refers to a mixture of mineral gold (Au) and sodium chloride (NaCl) from the 19th century. In the 20th century gold salts referred to gold thioglucose or gold thiomalate—neither of which was an actual salt.

Gold compounds, which can be ingested any number of ways, accumulate slowly in the body and, over time, reduce inflammation. Oral ingestion of gold is the least therapeutic method of introducing gold to the body. Today, gold, if ever used therapeutically is used to treat children with juvenile idiopathic arthritis who are unresponsive to non-steroidal anti-inflammatory drugs like methotrexate.

Gold is an expensive treatment.

## Is a 2nd Generation Gold Better Than Steroids or Small Molecules?

Arthrogen is not the only company working on a second or even third generation gold anti-inflammatory injection. Six years ago then Harvard post-doc researcher Brian DeDecker, who was searching for a new drug to treat autoimmune diseases, stumbled upon the biochemical phenomenon that explains gold's mechanism of action in the human body.

He published his eureka moment in the February 2006 issue of *Nature Chemical Biology*.

Dr. DeDecker wrote "Biochemical experiments indicate the metal-bound major histocompatibility complex (MHC) protein adopts a 'peptide-empty' conformation that resembles the transition

state of peptide loading. Furthermore, these metal inhibitors block the ability of antigen-presenting cells to activate T-cells. This previously unknown allosteric mechanism may help resolve how gold drugs affect the progress of rheumatoid arthritis and may provide a basis for developing a new class of anti-autoimmune drugs."

Specifically, Dr. DeDecker was tackling one of the key shortcomings of the small molecule approach to blocking the autoimmune response. To block it, any compound must disrupt certain specific MHC-peptide interactions. MHCs bind peptide antigens in endosomes and present them on the cell surface where they are recognized by CD4 T cells. But small molecule compounds (which are what most drugs are) have very hard time disrupting the tightly bound peptides and they tend to dissociate slowly from MHC proteins.

Autoimmune diseases, like rheumatoid arthritis, result when the body's immune system becomes over-active and can attack the body itself. There are approximately 80 separate autoimmune diseases which affect an estimated 25 million people annually in the U.S., of which the most common disease is RA.

## Available for Licensing

Dr. DeDecker, who is now with the University of Colorado, has continued to work on gold-based therapeutic compounds and is letting the world know that he has created gold compounds with higher affinity and specificity for treating RA. Since gold compounds work by displacing the autoimmune peptide from the MHC molecule, they address the root cause of autoimmune disease by disrupting immune cell recognition of self-peptides.

In effect, DeDecker has invented a form of antibody or aptamer which will interact with MHC-gold complexes to more efficiently (than either small molecule compounds or classic gold salts) prevent self-peptides from being recognized by the immune system.

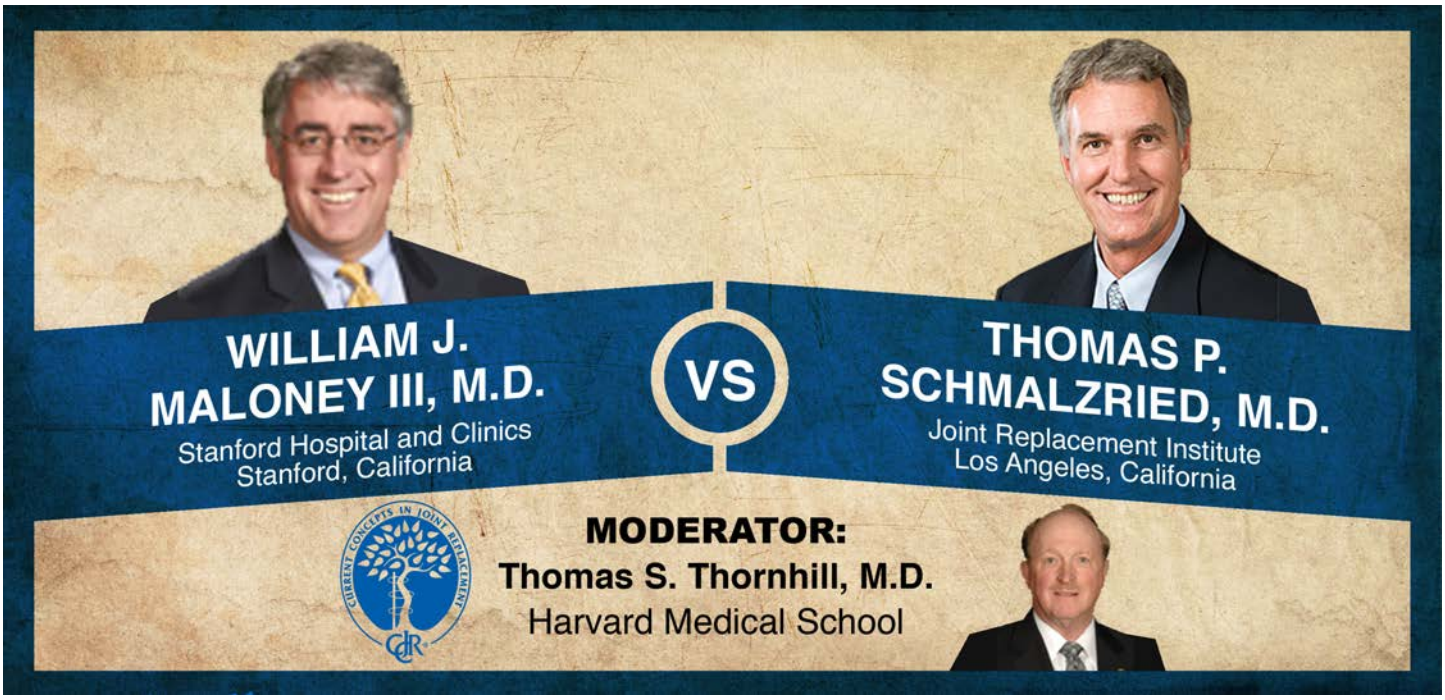
He believes his second-generation gold drugs will be more effective, more specific and less expensive that the classic gold salts, with fewer side effects for autoimmune diseases like RA. He also hopes to fine-tune these metal complexes into MHC class II allele specific molecules that could open up new platforms for the treatment of other autoimmune diseases including juvenile diabetes, multiple sclerosis, and lupus.

## GOLDIC and Other Gold Compounds

There is no question but that Arthrogen's novel approach to gold injections is extremely intriguing. Furthermore, Dr. DeDecker has looked at gold with fresh clinical eyes and he also has come up with some very interesting and valuable insights. Just taking a stab in dark here, but further research seems to be indicated. ♦

# Metal-Metal Articulation: Maloney v. Schmalzried

By Elizabeth Hofheinz, M.P.H., M.Ed.




*Current Concepts in Joint Replacement/RRY Photo Creation*

"Like taking candy from a baby," says Bill Maloney. "There is very little/zero indication for metal-metal articulations." "But the benefits of metal-metal are well known: high stability because of the large diameter, low wear potential, and they are unbreakable," states Tom Schmalzried.

This week's Orthopaedic Crossfire® debate is "Metal-Metal Articulation: Cease and Desist." For the proposition was William J. Maloney III, M.D. from Stanford Hospital and Clinics in Stanford, California. Against the proposition was Thomas P. Schmalzried, M.D. of The Joint Replacement Institute in Los Angeles, California. Moderating was Thomas S. Thornhill, M.D. from Harvard Medical School.

**Dr. Maloney:** "This is like taking candy from a baby. In the early to mid '90s we had terrible problems with osteolysis, especially in young, active patients with conventional polyethylene with cementless devices. Then new bearings were introduced: highly crosslinked polyethylene, metal-on-metal and ceramic-on-ceramic. The hypothesis was that if you reduce the wear volume it would mean a reduction in the incidence of osteolysis and the incidence of aseptic loosening."

"Ten years later: femoral component fixation is solved, and we're seeing unique complications with metal-metal articulations. There is a spectrum of adverse tissue reactions that have been described as a foreign body reaction; there's a toxicity reaction with cell necrosis, there's potentially a hypersensitivity reaction, and then there's ALVAL [aseptic lymphocytic vasculitis associated lesion]."

"In a paper from Oxford they showed this so-called pseudotumor formation with metal-metal resurfacings, and 1% of their patients developed symptomatic pseudotumors by five years… all females. The tumors were associated with extensive soft tissue necrosis, lower Oxford hip scores, and higher serum cobalt levels. One paper from Adolph Lombardi's group showed 3% cup failure, 11 local adverse tissue reactions, and 27 loose cups. This is unique to the large metal-metal total hip replacement."

"In one case from our institution there was a 65-year-old woman who presented with gross swelling of her right lower extremity. She has bilateral metal-metal total hip replacements. On the right the socket is abducted—not an optimal position—and the right was the affected side. On an MRI scan we could see the so-called pseudotumor tracking up the iliac wing, and the gross swelling of the leg."

"Another case: an implant that's supposedly had a good track record—metal-on-metal and a relatively small bearing surface. Several years ago looked at this in culture, and examined the difference between cobalt, chromium, titanium, and titanium aluminum. We did serial dilutions and exposed cells to these materials in culture; we found a fundamental difference between titanium and cobalt. Titanium was inflammatory and led to a typical inflammatory foreign body type reaction, with secretion of bone resorbing cytokines; at the same particle concentration cobalt killed the cells."

"Remember that there's a higher rate of cobalt ions. Cobalt is relatively soluble, whereas titanium and the other metals are relatively insoluble. When you look at revisions for metal-metal failures, the outcome is poor in general as compared to revision for femoral neck fracture resurfacing. And with revision for soft tissue reaction the outcome is poor. If you look at data from the Australian registry—28 mm heads or smaller—and adjusted for age and gender, you can see the worse outcomes at the five-year point were metal-metal. The best were metal-polyethylene. If you look at large heads, same outcome…worse for metal-metal and best for metal-highly crosslinked polyethylene.

"If you examine the English registry and examine implant survivorship in their hands, cemented total hip replacements do the best, followed by cementless and hybrid hip replacements; the worse were hip resurfacings and large head metal-metal total hip replacements. So in 2011 there is very little/zero indication for metal-metal articulations."

**Dr. Schmalzried:** "The benefits of metal-metal are well known: high stability because of the large diameter, low wear potential, and they are unbreakable. The thin monoblock sockets allow for resurfacing with acetabular bone conservation. One of the risks is a higher loosening rate…and loosening is more of an issue than adverse local tissue reaction. Another is that there is position sensitivity. In addition, metal particles, ions, corrosion products, adverse local tissue reactions are a problem as well."

"Hip dislocation is the number one reason for revision in the Medicare data set. A typical issue was having a 28 mm poly case that was dislocated…that is the kind of experience that drove the market in the direction of larger heads. And the largest head options were metal-metal, and the very largest options were monoblock sockets against very large heads."

"You can end up with an exposed mass of metal in the front of the hip joint, and a large head-neck gap because of the drop off between the edge of the head and the neck. This has been associated with groin pain, psoas symptoms, but is it due to soft tissue inflammation or the stiffness of the cobalt chrome socket? There also seems to be an increased incidence of modular taper corrosion in association with large diameter metal-metal bearings."

"The Australian data indicates that loosening is the problem, as opposed to adverse local tissue reaction. Don't think that I'm not concerned about the latter, but loosening is associated with the larger heads and the monoblock sockets. In this registry the cause of revision is 0.5% metal sensitivity."

"Monoblock sockets allow very large heads, but they can be more difficult to insert. Also, there's no opportunity for adjuvant fixation such as screws, and they may not bone-ingrow."

"In the 2010 Australian National Joint Registry they had greater than 96% five-year survival of modular metal-metal constructs. Large is forgiving…for stability. But it is no more forgiving of position. There are growing numbers of studies showing that if you have a metal-metal bearing or any hard-hard for that matter, that has a lateral opening angle of greater than 50-55 degrees then you are likely to have a wear related problem. The same thing has been shown by at least one observer with version outliers—too much anteversion or too little anteversion."

"The concept of the bearing coverage area relates to both the acetabular and femoral positions; it's a fundamental parameter, and it's position and component design. Also, component position recognition is a current issue."

"Our own investigations have shown the common denominator to be the path mechanics of that joint. Low lateral opening angle or high combined anteversion leads to edge loading, edge wear and aberrant wear mechanism and an adverse local tissue reaction. Crosslinked polyethylene is now available in larger diameters; that's going to lower the dislocation risk. The downsides: fracture risk because the liners are thinner, higher volumetric wear (will that matter over time), and there is the potential for in vivo oxidation."

"Perhaps antioxidant polyethylene is the way to go—time will tell. We need longer term data on crosslinked polyethylene with equivalent head size and diameter. Delta-delta has been approved for 28 mm, but that's not going to help us much with the range of motion and stability issue."

"The majority of my metal-metal experience is with hip resurfacing. The patients I care for are unaccepting of disability and they want no restrictions. The requirements include substrate strength, range of motion and stability, low wear and revisability. There are learning issues, but Treacy's experience (2010) shows 98% 10-year survival for males and 96% 10-year aseptic survival for all comers. In the 2010 Australian registry they had greater than 96% survival in males younger than 65 with osteoarthritis, and greater than 96% survival when you have a large patient."

"In my opinion the benefits still outweigh the risks in appropriate patients."

**Moderator Thornhill:** "Thirty second rebuttal, Bill?"

**Dr. Maloney:** "I focus on the adverse tissue reactions because once you get one you may not recover. Tom has said that not only do we have problems with adverse tissue reactions, we have a very high failure rate as it relates to socket fixation…and it's technically more difficult to put in. As it relates to activity level, Tom, your own data suggests that it's a patient selection issue with resurfacing...that you have patients who have come in who are of that mindset who are not candidates for resurfacing and had total hip replacements and have had high activity levels. So it's not accurate to attribute the activity level to the implant."

**Dr. Schmalzried:** "I agree. I think we've come to a point where we are very risk averse, but my experience has been overwhelmingly favorable with regard to metal-metal resurfacing."

**Moderator Thornhill:** "Tom, should we do metal-metal in a non-resurfacing situation?"

**Dr. Schmalzried:** "In a total hip, probably not."

**Moderator Thornhill:** "Bill, what's the best way to diagnose this?"

**Dr. Maloney:** "Ultrasound or CT, depending on your institution. I think hip aspiration plays a valuable role; if you examine the fluid, with an adverse tissue reaction it usually has a very low white cell count…and if there is an infection it will have a high white cell count."

**Moderator Thornhill:** "How about measuring serum cobalt chromium levels?"

**Dr. Maloney:** "We're doing this on all patients who come in with a painful metal-metal; what these measurements mean is yet to be determined. I think there's an association with higher metal ion levels and adverse tissue reaction, but it's not a one-to-one correlation."

**Moderator Thornhill:** "Who do you measure levels in, Tom?"

**Dr. Schmalzried:** "On anybody that wants to be checked, and anybody who's not perfect. You take someone who's having some symptoms or a component position issue, the likelihood that patient will have elevated ions is increased. And if there's a concern, then do an imaging study. The workup is cookbook."

**Moderator Thornhill:** "Let's say you have a patient who is asymptomatic, but wants the levels done…and they're elevated."

**Dr. Schmalzried:** "I would get a MARS MRI scan. I am looking to see if there is a local tissue reaction."

**Moderator Thornhill:** "Bill, same thing?"

**Dr. Maloney:** "Yes."

**Moderator Thornhill:** "Are we dealing with a local toxicity or type 4 hypersensitivity, or are they both in different clinical situations?"

**Dr. Schmalzried:** "There is a spectrum of soft tissue reactions. In some cases it looks like a foreign body reaction; with the ions I think there's a toxicity and the lymphocytic infiltrate may be related to some type of hypersensitivity reaction."

**Moderator Thornhill:** "Tom, what is a large head? Above 36?"

**Dr. Schmalzried:** "Thirty-six has been the cutoff point that registries have used. But that mixes modular systems with monoblock systems and that muddies the waters."

**Moderator Thornhill:** "Bill, the court of public opinion…how should we, as academic leaders of orthopedics, respond to that?"

**Dr. Maloney:** "It's hard to respond because they have the pulpit. Tom?"

**Dr. Schmalzried:** "There are societal forces that are driving perception. If you have a patient with a cobalt chrome total knee replacement and you measure their cobalt and chromium ions, you're going to have 2-3 parts per billion in that patient. It's not just an issue of metal-metal bearings, so the issue of exposure (dose, cause, and effect) becomes very important."

**Moderator Thornhill:** "I think we have a consensus that we wouldn't advocate using metal-metal in a total hip, but limit it to those people who require resurfacing. Thank you." ♦

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# Gluing the Annulus! More ICU Better for High-Risk THA?…Orthopedic Literature: Cut Through the *&^%$

By Elizabeth Hofheinz, M.P.H., M.Ed.

**Gluing the Annulus** Repairing the annulus after a micro discectomy is not a new idea. But using glue (specifically fibrin glue) just might be. James Iatridis, Ph.D. and his team have been focusing their efforts on furthering the status of annulus fibrosus repair. They are particularly hoping to find solutions for those who have herniations and who undergo micro discectomy. Dr. Iatridis, director of spine research at the Mt. Sinai School of Medicine, tells *OTW*, "The goal should be not just to take away the herniated tissue, but to repair the annulus. We have just published two review articles describing the status of annulus fibrosus repair. In the first paper we describe what needs to be repaired biomechanically and strategies for repairing the injured intervertebral disc with different biomaterials. Our concept is that we must restore both annulus fibrosus integrity (detectable with torsional measurements) and nucleus pulposus pressurization (detectable with intradiscal pressure or axial biomechanics measurements)."


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"In these articles we describe what an injury to the annulus fibrosus does to the biomechanics and the biological environment, as well as ways to characterize that injury. For example, a puncture in the annulus fibrosus results in a loss of pressurization of the disc. Contrast this with a herniation where there is a greater disruption in the annulus fibrosus. We're screening different treatments in the lab for degenerative disc disease. Our organizing principle for annulus repair is to achieve three design criteria: the material must mechanically match the native material properties of the annulus fibrosus, support the growth of intervertebral disc cells, and be strongly adherent to seal annulus fibrosus defects under physiological strain levels."

"At the recent Orthopaedic Research Society (ORS) meeting in San Antonio, we presented two abstracts characterizing our fibrin-based biomaterial which shows promise as an annulus fibrosus sealant. In the first, we enhanced our formulation of a Fibrin-Genipin adhesive with the addition of cell adhesion molecules for improved cell growth. This gel is exciting because it meets our design criteria and it doesn't degrade as quickly as unmodified fibrin gels. The second abstract described our characterization of this Fibrin-Genipin adhesive in a novel organ culture model, demonstrating biomechanical restoration, strong adhesion with the native tissue, and transport of annulus fibrosus cells from the native tissue into the gel. Given our promising results, we will pursue animal model testing and hope these studies of annular repair will translate to therapies for lumbar microdiscectomy patients that minimize both the likelihood of reherniation as well as further disc degeneration."

**More ICU Better for High-Risk THA?** Yes! Says the winner of the 2012 OREF (Orthopaedic Research and Education Foundation)/CCJR (Current Concepts in Joint Replacement) Clinical Practice

Award. Atul Kamath, M.D., who is completing a fellowship at Mayo Clinic in Rochester, Minnesota, tells *OTW* about his study on unplanned ICU following THA (total hip arthroplasty). "Elective hip and knee arthroplasty is a safe procedure, but the risks of morbidity and mortality are real, with certain risk factors more highly associated with postoperative complications. We wanted to identify those patients who are more at risk and to find out how to shepherd them through the system along safe pathways. This was a two-part study: in the retrospective portion, we looked at a large number of patients and developed a model for risk that included age, revision surgery, body mass index, prior myocardial infarction, and creatinine function. We found that with each risk factor, there is an inherent risk of unplanned ICU admission post-operatively; and, as you combine risk factors, the risk increases dramatically."

"In the prospective part of our work, we took those patients who were at the highest risk and sent them to the ICU immediately after surgery to see if it made a difference. In fact, this did decrease mortality and unplanned admissions. But, of course, there remains a resource allocation issue—we cannot send all high-risk patients to the ICU at a tertiary referral center. So now we aim to fine-tune the model to ensure that we are sending only the most high risk patients as identified by our modeling. There is also the opportunity to gather data post-discharge, such as readmission rates and other factors important in our current healthcare climate. Over the next six months, we will focus on developing metrics for cost. We would also like to track our initial prospective THA cohort for 6-12 months and get a sense of how they doing, as well as comparing these patients to those who did not go through our triage system."

**Orthopedic Literature: Cut Through the *&^%$** Tired of wading through piles of journals? Simplicity has arrived…and it is called OrthoEvidence (www.myorthoevidence.com). Mohit Bhandari, M.D., Professor and Research chair in Orthopaedic Surgery at McMaster University in Canada is making orthopedists lives substantially easier. Dr. Bhandari tells *OTW*, "At the end of the day, if there is no way for us to get reliable high quality information to surgeons in a timely way, research in journals has little impact. OrthoEvidence (OE) is designed to bridge the gap between quality evidence and current medical practice, a real issue when there is so much literature being released each month. Our process is rigorous, and involves scanning 40 journals monthly. We look for the best evidence, sum it up, do a critical appraisal, and create what we call an Advanced Clinical Evidence (ACE) report. We are focusing on high quality evidence from randomized clinical trials and meta-analyses; and while high impact journals like *Journal of Bone and Joint Surgery* (JBJS) remain trusted resources for orthopedic surgeons, they publish only a fraction of the best evidence in our field around the world. This means that the average orthopedic surgeon is missing out on practice changing information."

"Thus far we have partnered with 25 leading orthopedic association and societies from around the world. OE is being accessed in over 170 countries by over 30,000 orthopedic surgeons. With over 1,250 ACE reports in our database we are happy to be making the daily lives of orthopedic surgeons run more smoothly."

**Biomarkers for Osteoarthritis: Where Are We?** Using the model employed by the Foundation for the National Institutes of Health (FNIH) in the development of biomarkers to monitor harmful effects of drugs on the kidney, osteoarthritis researchers are making critical steps to advance methods to facilitate the development of effective osteoarthritis treatments. Virginia Kraus, M.D., Ph.D., professor of Medicine in the Division of Rheumatology at Duke University Medical Center, is co-leading the effort with Dr. David Hunter, professor of Medicine at the University of Sydney in Australia, to validate biochemical and imaging markers for osteoarthritis (OA). She tells *OTW*, "We continue to work with industry and the FNIH to find biomarkers that predict disease progression. The study is going well and we will present our first abstract in April 2013 at the Osteoarthritis Research Society International. That work shows the predictive capability of imaging biomarkers from MRIs related to changes in the morphometry of the knee. We are seeking additional funding partners for this work as well as additional cohorts to validate the results. Studies demonstrating a structural modification of OA, such as a recent trial from Europe, may help with the further qualification of markers. Everyone we speak with agrees that this work is vital to making advances in osteoarthritis treatment."

**Andrew I. Spitzer, M.D.: New Member of Israel Orthopaedic Association** Dr. Spitzer, director of the Joint Replacement Program at the Cedars-Sinai Orthopaedic Center in Los Angeles, is being recognized for his work in Israel. He has traveled to that country more than a dozen times to share his knowledge with local surgeons, often treating patients for free. In a gesture of appreciation, the Israel Orthopaedic Association has made Dr. Spitzer an honorary member. ♦

company

## Rockford and Crystal Lake to Merge

Rockford Orthopedic Associates and Crystal Lake Orthopedics, two specialty health care organizations in northern Illinois, have announced their intent to merge and have entered into a due diligence process. The merger is slated to be completed in the fall of 2013, after which time the organizations will utilize their combined resources to expand their subspecialty services offered to patients.

Each clinic will be recruiting skilled staff and physicians, improving technology and enhancing customer service. Both parties indicated that the merger will also help the organizations expand subspecialty services to residents in the entire northern Illinois region. While Crystal Lake Orthopedics will be merged into Rockford Orthopedic Associates, the clinic name will not change. Current providers will also remain in Crystal Lake so there will be no disruption in patient care. The physicians at Crystal Lake Orthopedics will also maintain their current hospital privilege designation and call coverage.

Ed Grogg, CEO of Crystal Lake Orthopedics told *OTW*, "Our first few steps include due diligence work on the legal side of the merger. Also, bringing leadership together from both entities to work through the operation challenges. The biggest challenges are keeping organized with all the issues that need [to be] addressed and proceeding forward without disrupting current operations. Both Crystal Lake Orthopedics and Rockford Orthopedic Associates still have to run practices and make sure our physicians and employees don't lose focus."

After the merger is finalized, Grogg will continue in a leadership role as the new Chief Operating Officer and will maintain his office in Crystal Lake to provide oversight of daily operations.

Don Schreiner, CEO of Rockford Orthopedic Associates commented to *OTW*, "In addition to bringing leadership together to work through detailed due diligence review we need to methodically layout our post-merger implementation activities including streamlining business operations, staff integration, facilities planning, and provider recruitment. We must immediately begin to blend the corporate culture for physicians, mid-level providers, and staff and define who we want to be."

*—EH (February 6, 2012)*

*Image created by RRY Publications, LLC. Source: Wikimedia*

# Smith & Nephew Cuts Jobs, Blames Taxes

Smith & Nephew (SNN) is laying off almost 100 workers at its plants in Memphis, Tennessee, and Andover, Massachusetts.

On January 31, 2012 a company statement said the positions had been made "redundant across various departmental functions," because the company is not immune from the added expense burden of the 2.3% medical device tax. No further explanation was given of how the new taxes made the positions redundant.

"The nearly $30 billion tax on medical devices that took effect January 1, 2013, has impacted a number of companies across the U.S.," the company said in a statement to a local television station.

The *Memphis Daily News* reported that sources familiar with the job cuts say it included about 60 Memphis employees from the Advanced Surgical Devices division at the company's Goodlett Farm Parkway facility.

Jo Metzger, senior vice president of corporate communications, said the company is providing the affected employees with a comprehensive severance package and outplacement support."

Smith & Nephew employs an estimated 1,815 people in Memphis, according to *Memphis Business Journal* research.

### Company Restructuring

About a year ago, the company announced that it was reducing its global workforce by 7% over the next three years. In 2012, the company merged its orthopedic reconstruction unit based in Memphis with its advanced wound management, sports medicine and trauma unit is based in Andover. Both locations saw job cuts in December 2011 in a move to eliminate duplicate positions and the continued restructuring of Smith & Nephew. The Memphis location cut about 80 positions.

The president of the Memphis division, Joseph DeVivo, left the company that August as Mike Frazzette in Andover became president of the new division.

For the third quarter 2012 the company reported revenues of $952 million compared to revenues of $1.03 billion in the third quarter of 2011.

### Other Memphis Job Cuts

The layoffs in 2011, reported *The Daily News*, came late in a year that had already included jobs cuts by its competitors—Medtronic Inc. and Wright Medical—which both also have facilities in Shelby County.

Wright is based in Arlington and Medtronic's spinal and biologics business is based in Memphis.

Last summer Medtronic cut 500 positions, and another 500 are expected by the end of 2013. In March 2010, Medtronic had warned that taxes relating to the new health care reform could result in a reduction of about 1,000 jobs.

*The Daily News* story noted SNN bought the Goodlett Farms Parkway property in January 2010 as part of a $42 million expansion of the global headquarters for the then-orthopedics division.

### Local Tax Incentives

In December 2009, the Memphis Shelby County Industrial Development Board approved a $6.2 million payment-in-lieu-of-taxes agreement with Smith & Nephew for the Goodlett Farms expansion, which the company said would create 160 jobs and generate $13 million in annual payroll at an average annual wage of $93,427 excluding benefits.

*—WE (February 6, 2013)*


*Courtesy: Smith & Nephew*

# Zyga Completes Glyder Trial Enrollment in Europe

Zyga Technology, Inc. has completed enrollment in the Glissade trial to demonstrate performance of facet resurfacing.

"For patients suffering from chronic facet pain, there has never been a viable procedure providing long term relief," said Professor Dr. Hans Jorg Meisel, M.D., director of the Center of Neurosciences of the BG-Clinic Bergmannstrost Halle, Germany and principal investigator for the study. "Their options were to receive injections several times each year or to undergo a more aggressive, permanent spine fusion procedure. The Glyder system offers simple, minimally invasive implantation of a device designed to preserve the patient's anatomy and to provide long-term pain relief. Our initial patients are now reaching two years post-surgery, and we are very encouraged to see that they are experiencing sustainable pain relief."

When the study began in August 2011, Dr. Meisel noted the Glyder was very easy to implant into the facet joints. Brazilian spine surgeon, Luiz Pimenta, M.D., medical director, Instituto de Patologia da Coluna, Sao Paulo, Brazil, the first surgeon to implant the device said, "Early results (in 2011) suggest that Glyder could be a good option for treating patients suffering from facet pain," and was looking forward to results from the European study.

**Clinical and Economic Value**

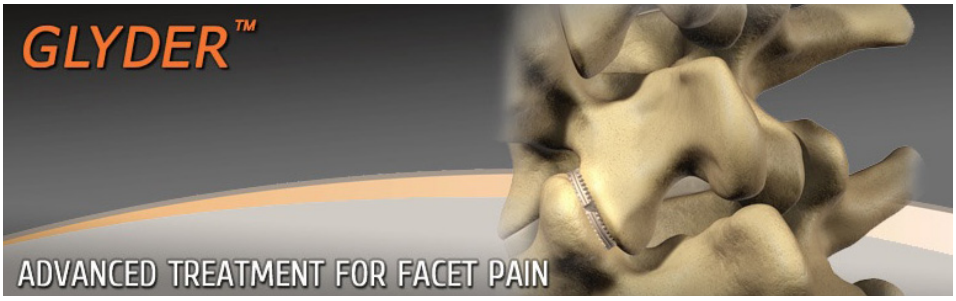
The preliminary results, "suggests the Glyder system's clinical and economic value," said company President and CEO Jim Bullock on January 31, 2013.

Over 31 million people in the U.S. suffer from chronic low back pain. Approximately 31% of that chronic back pain is attributable to the face joints, according to the Centers for Disease Control.

A company statement says the prospective, 40-patient trial is studying the Glyder Facet Resurfacing System in the treatment of chronic facetogenic pain. Preliminary data analyses from this five-site trial indicate a significant reduction in pain and improvement in function as measured by Visual Analogue Pain Scale (VAS) and Oswestry Disability Index (ODI). The results of this trial will serve as the foundation for future investigation including the DUET Clinical Trial in Europe and the U.K., and mid-2013 submission for an Investigational Device Exemption (IDE) Study to the U.S. Food and Drug Administration (FDA). The company anticipates CE Marking approval in late 2013.

Zyga Technology, headquartered in Minneapolis, is currently marketing the Simmetry Sacroiliac Joint Fusion System, a minimally invasive procedure intended for conditions including sacroiliac joint disruptions and degenerative sacroiliitis.

*—WE (February 5, 2013)*




*Glyder/Zyga Technology*

large joints

# Sunlight Wards Off RA?

Elizabeth V. Arkema, M.D., of Harvard School of Public Health and Brigham and Women's Hospital in Boston, along with colleagues, is shedding light on the role of sunlight in rheumatoid arthritis (RA). Her study found that regular exposure to sunlight—specifically ultraviolet B (UV-B)—may reduce the risk of developing the disease.

*Wikimedia Commons and Arivumathi*

The researchers used data from the U.S. Nurses Health Study (NHS), the first of which has tracked the health of more than 120,000 nurses since 1976, when they were aged between 30 and 55, until 2008. The second (NHSII), has tracked the health of a further 115,500 nurses since 1989, when they were aged between 25 and 42, until 2009.

The team went beyond using geography alone to quantify likely levels of UV-B exposure; they utilized a more sensitive assessment, known as UV-B flux, which is a composite measure of UV-B radiation, based on latitude, altitude, and cloud cover. Exposure was then estimated according to the U.S. state of

residence, and ranged from an annual average of 93 in Alaska and Oregon to 196 in Hawaii and Arizona. Likely estimates of UV exposure at birth and by the age of 15 were also included.

Over the study period, 1,314 women developed RA. Among nurses in the first NHS cohort, higher cumulative exposure to UV-B was associated with a reduced risk of developing the disease. Those with the highest levels of exposure were 21% less likely to develop rheumatoid arthritis than those with the least, the analysis showed.

This supports the findings of other studies, showing a link between geography and the risk of rheumatoid arthritis as well as other autoimmune conditions, including type 1 diabetes, inflammatory bowel disease, and multiple sclerosis. But the authors of this study found no such association for UVB exposure among women in NHSII, who were younger than those in the first NHS, and might have been more savvy about the potential hazards of acquiring a tan.

"Differences in sun protective behaviors (e.g., greater used of sun block in younger generations) may explain the disparate results," stated the authors in the February 4, 2013 news release.

Dr. Arkema told *OTW*, "We were most surprised to learn that a higher average UV-B exposure was associated with a 21% decreased risk of rheumatoid arthritis in an older cohort of women, but not in the younger cohort. This is the first study using area-level UV-B measurements to examine this association, and these results may be considered preliminary. Future studies should examine dose and time of exposure and take into account use of sunscreen and time spent outdoors."

*—EH (February 8, 2012)*

## Dairy Varies in Promoting Bone Strength

Aching hip? Try milk or yogurt. (But that won't help your spine.) New findings from the Institute for Aging Research (IFAR) at Hebrew SeniorLife, an affiliate of Harvard Medical School, show that dairy—specifically milk and yogurt—is associated with higher bone mineral density (BMD) in the hip, but not the spine. Their "cousin," cream, may be associated with lower BMD overall. The authors indicate that these findings suggest that not all dairy products are equally beneficial in promoting bone strength.

"Dairy foods provide several important nutrients that are beneficial for bone health," says lead author Shivani Sahni, Ph.D., Musculoskeletal Research Team, IFAR, in the February 1, 2013 news release. "However, cream and its products such as ice cream have lower levels of these nutrients and have higher levels of fat and sugar. In this study, 2.5 to 3 servings of milk and yogurt intake per day were associated with better bone density. More research is needed to examine the role of cheese intake (some of which can be high in fat and sodium), and whether individual dairy foods have a significant impact in reducing fractures."

IFAR researchers utilized data collected from a food frequency questionnaire completed by 3,212 participants from the Framingham Offspring study. They then compared participants' dairy intake with BMD measurement, which revealed the benefits of milk and yogurt versus cream in largely middle-aged men and women. According to the study, nutrient composition varies among dairy foods. Choosing low-fat milk or yogurt over cream can increase intake of protein, calcium and vitamin D while limiting intake of saturated fats.

*—EH (February 6, 2012)*


*Wikimedia Commons and Darekm135*

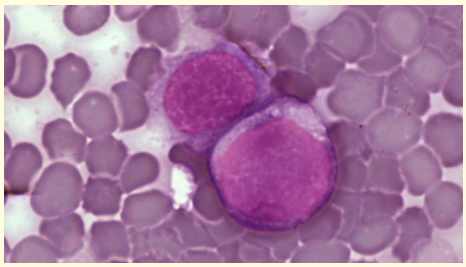
## Synovium Stem Cell Shots Delay Cartilage Degeneration

The synovium is the thin membrane that covers the inside of hip and knee joints. Now researcher Nobutake Ozeki, of Tokyo Mental and Dental University in Japan, with his colleagues, has found that periodically injecting stem cells from the synovium into knee joints may delay cartilage degeneration.

The researchers began by injecting synovium stem cells into the knees of rats with osteoarthritis and found that the injections did delay the degeneration of the rat's cartilage. The hope now is that these injections could provide osteoarthritis patients with relief from the often debilitating effects of the disease. *PR Newswire* quotes Ozeki as saying, "Stem cells can change their character according to the environments and produce a variety of growth factors. We previously revealed that stem cells from synovium have advantages for their high growth and cartilage differentiation abilities."

The goal of his research, he explained, is to provide patients with an alternative to surgery. "We want to improve patient's joint condition without surgical interventions and using stem cells is one possible alternative treatment," he said.

In a continuation of his research, Ozeki and his team plan to try this therapy



*Wikimedia Commons and Ayacop*

on more severe osteoarthritis models in which cartilage degeneration has already begun. "In the future," Ozeki said, "we want to start a clinical trial to delay osteoarthritis progression." Ozeki presented the results of his research at the Orthopaedic Research Society's 2013 Annual Meeting in San Antonio, Texas.

*—BY (February 5, 2013)*

## Cole Tests Novel Stem Cell Therapy for Cartilage Repair

The country's first clinical trial of the stem cell drug, Cartistem, designed to repair knee cartilage damaged by aging, trauma or degenerative diseases, is underway at the Rush University Medical Center. According to the university's press release, Cartistem is made from mesenchymal stem cells derived from umbilical cord blood that has been supplied by donors. Umbilical cord blood is a readily accessible source of high-quality stem cells, has minimal health risks and carries relatively few ethical concerns. The cells are mixed with hyaluronan, a natural polymer that plays a major role in wound healing and is a building block of joint cartilage.

Brian Cole, M.D. a professor in the department of orthopedics and anatomy and cell biology at Rush University Medical Center is the principal investigator. Cole is also head of Rush's Cartilage Restoration Center. He and his associates have taken on a major challenge in orthopedics as cartilage damage has long resisted attempts to repair it. The tissue lacks blood vessels and nerves and so has little capacity to regenerate itself.

*Brian Cole, M.D.*
*Rush University Medical Center*

"Finding a biological solution for cartilage regeneration in orthopedics is one of the fastest growing areas of research and development in our specialty," said Cole. "Rush is spearheading this field of research with the ultimate goal of safely improving outcomes and sparing patients from having more complicated surgery at a relatively young age."

The Phase I and II study is planned to last for two years and will enroll twelve participants age 18 and older with a body mass index of less than 35. The plan is to enroll six participants with cartilage lesions of from two to five centimeters and six more participants who have lesions larger than five centimeters. All 12 will be followed up for a year, to determine the safety and efficacy of the drug, and will be evaluated again at the end of two years.

"With a burgeoning aging, yet active population, our patients are looking for effective non-joint replacement solutions to treat their damaged knee cartilage," said Cole. "This research is significant in that it utilizes a commonly performed operation (microfracture) in an effort to improve upon variable outcomes." He added, "Notably, this is a treatment for patients with localized cartilage damage and not for patients who are diagnosed with diffuse or bone on bone arthritis who have otherwise been told they require a knee replacement."

*—BY (February 5, 2013)*

# Remote Monitoring Technology Developed for Joints

*PR Newswire* reports that JointMetrix Medical, LLC has developed novel remote monitoring technology to use in conjunction with joint replacement surgery. The company described the workings of the technology at the recent 2013 meeting of the Orthopaedic Research Society in San Antonio, Texas. JointMetrix Medical's remote monitoring technology enables continuous and accurate measurement of patients' joint motion and overall activity. According to company officials, this represents a breakthrough in clinicians' ability to track and positively influence post-surgical outcomes.

The system was developed by JointMetrix Medical in collaboration with a team of clinicians and researchers at University of Washington's Department of Orthopaedics and Sports Medicine. Several leading U.S. orthopedic centers are preparing research initiatives that leverage the system, which the company expects to be commercially released later in 2013.

"Remote monitoring will be an important element of care in Orthopaedics, allowing clinicians to more appropriately select and care for their patients," said Dave Marver, CEO, JointMetrix Medical. "The data our system provides will allow earlier and more effective intervention while providing much needed efficiencies for busy surgeons and their staffs."

JointMetrix Medical, LLC was created to commercialize technology developed by Peter Cavanaugh, Ph.D., former chairman of Biomedical Engineering at Cleveland Clinic and current vice chair for research in the Department of Orthopaedics and Sports Medicine at University of Washington. Cavanagh developed JointMetrix Medical's underlying technology over the last decade in connection with NASA-sponsored research to measure astronauts' activity aboard the International Space Station. The company is pioneering clinical use of remote monitoring in orthopedics.

*—BY (February 5, 2013)*

*Courtesy of JointMetrix Medical, LLC*

## biologics

# Stem Cells Grow New Nose

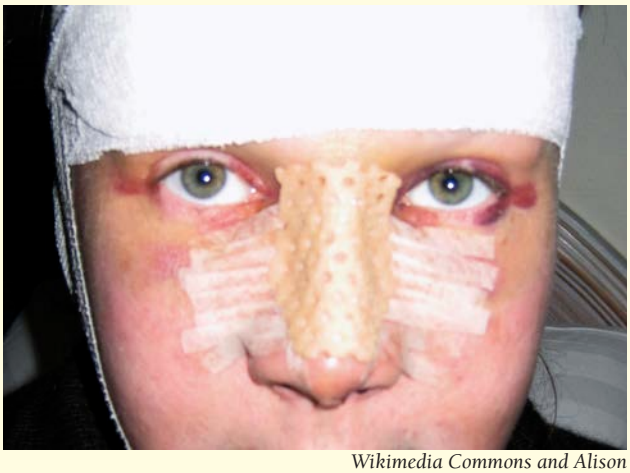
The British are at it again—first a trachea and now a nose. The *BBC Focus* magazine recently profiled the work of Professor Alex Seifalian, of University College, London, who is leading a team to create a new nose for a London businessman who lost his original nose to cancer. The trial, if successful, will be the first time a full nose will have been grown from stem cells.

Seifalian first created a glass model of the man's nose and spayed it with honey-comb shaped material to form a biological scaffold for new cells to attach to. Once the scaffold had been created the researchers removed the glass mould and coated the biological frame with millions of stem cells. While the scaffold was being built, the researchers inserted a small balloon beneath the surface of the man's arm and gradually inflated it to stretch the skin, making it loose enough to accommodate the new nose.

Two months ago, doctor's removed the balloon from under the skin and in its place inserted the nose framework where it now resides in the man's arm growing new networks of nerves, blood vessels and skin. Researchers believe that, if all goes well, after three months beneath the skin on his arm, the nose will be ready to be removed. Once it has been removed doctors will surgically reattach the nose to the man's face. They will also sew up his arm and it should return to normal.

Seifalian said the man's nose has been designed to look exactly like the original—slightly crooked. He told *BBC Focus* magazine: "His nose was a little bit bent to the left and we asked if he wanted it straight but he said no, he wanted it exactly the same."

*—BY (February 5, 2013)*



*Wikimedia Commons and Alison*

## extremities

# FDA Clears Conventus DRS Implant

Conventus Orthopaedics, Inc. a privately held company focusing on treatment for peri-articular fractures, has received 510(k) clearance from the FDA to market its Conventus DRS implant within the United States. The implant is designed to provide a less invasive means to treat patients with distal radius fractures—hopefully returning them to daily activities sooner and with less pain.

According to the Conventus literature, the DRS technology provides clinicians with a unique, self-expanding implant

CONVENTUS orthopaedics

*Courtesy of Conventus Orthopaedics, Inc.*

that stabilizes the fracture fragments from within the bone. The surgical procedure requires only a two to three centimeter incision on the forearm and a few tiny incisions at the wrist. The technique reduces surgical trauma by as much as 80% compared to traditional plate and screw fixation techniques. The technique preserves soft tissues around the fracture to minimize stiffness, swelling, and pain. Company officials say the DRS implant represents the first minimally-invasive, fragment-specific system that effectively addresses a wide range of fracture types with fixation stability equivalent to traditional plates and screws.

Reporting on a 60 patient multi-center European clinical study, Michael Strassmair, M.D., the principal investigator, said, "In Stamberg we used the Conventus DRS implant successfully in over 30 patients. We have been able to successfully treat a broad range of distal radius fractures using the system and see significant advantages in comparison to volar plating. Early pain relief for patients has translated into the early mobility necessary for rapid recovery."

The company takes its name from the Latin word for coming together or union, Conventus Orthopaedics is focused on creating less invasive solutions to fractures in and around joints. It is located in Minneapolis, Minnesota.

*—BY (February 5, 2013)*

trauma

## Ultrasound Bone Healing Costs Less Says NICE

*Courtesy of Exogen.com*

The British health agency, the National Institute for Health and Clinical Excellence (NICE), has announced that it supports the use of an ultrasound bone healing device as an alterative to surgery for fractures that are slow to heal. In a press release the NICE stated that, "the available clinical data on the effectiveness of EXOGEN for treating long bone fractures with non-union show high rates of fracture healing."

NICE also examined the manufacturer's claims that there could be cost benefits from using EXOGEN more widely in the National Health Service (NHS) and found, "EXOGEN is cost saving compared with current management for the treatment of non-union." England's National Health Service established NICE to provide evidence-based guidance about medicines, treatments, procedures and devices that represent the best quality care and which offer the best value for the money for NHS.

EXOGEN uses an ultrasound signal to stimulate broken bones to heal naturally. Manufactured by Bioventus LLC, the product has been used worldwide since 1997 and, according to the firm's press release, is the market leader in the U.S. for fracture stimulation.

Patients using EXOGEN place an ultrasound probe on the skin for 20 minutes a day and the treatment, done at home, is pain free. According to Bioventus, there are no known side effects. Bioventus' clinical studies have shown EXOGEN to have an equivalent 86% success rate as surgery. EXOGEN's use in the NHS has, reportedly, been inconsistent with some UK doctors having to persuade hospital managers to fund it.

*—BY (February 5, 2013)*

reimbursement

## Device Makers Passing on Device Tax

Now that the first $97 million of the new device tax has been collected by the government, it raises the questions of who is paying the price of the 2.3% tax.

We've seen numerous reports that thousands of laid-off workers from device companies have paid for the tax with their jobs. Other reports from device makers say that cuts to research and development budgets means patients who will not receive new treatments will suffer.

*tableatny/Wikimedia Commons*

**Purchasers Alarmed**

Now hospital purchasing groups are complaining that some device companies are attempting to pass the new tax on to them.

On January 25, 2013, the Healthcare Supply Chain Association (HSCA) and its group purchasing organization (GPO) members expressed alarm over evidence that some medical device manufacturers are shifting the burden of the medical device excise tax directly to American hospitals and other healthcare providers.

HSCA President Curtis Rooney said, "It is disheartening to find that some medical device companies have chosen to tack the tax right onto their invoices. We urge all manufacturers to immediately stop passing the medical device tax on to American hospitals, and ultimately to patients and taxpayers."

"American hospitals have already lived up to their shared financial responsibility for national health care reform," added Rooney.

Hospitals say they've already kicked in $155 billion in the form of Medicare-payment cuts over ten years to help pay for the health law and that other sectors should pay their share. "We're disappointed," said Mike Rock, senior associate director for federal affairs at the American Hospital Association (AHA). Last March, HSCA, AHA, the Federation of American Hospitals, and the Catholic Health Association urged the Internal Revenue Service to draft rules to prevent manufacturers from passing on the cost of the device tax to hospitals.

**Invoices Scrutinized**

On January 25, *The Wall Street Journal* reported on a review of letters and invoices from nine manufacturers sent to hospitals.

One letter sent by Carica, Inc., a maker of heart surgery tools, stated, "As a result of this law, we will be forced to charge the 2.3% federal medical device excise tax to you." Invoices from companies including feeding-tube supplier Applied Medical Technology Inc. and respiratory-valve maker Hans Rudolph Inc. added new surcharges or warned hospitals of price increases to cover the new tax.

The *Journal* reported that Adam Robinson, a contract manager at Beth Israel Deaconess Medical Center in Boston noticed a new 2.3% surcharge—labeled as a "medical device adjustment"—in a bill for radiology supplies sold by a small company. Procurement officials say they have seen the charges appended to commodity items sold by "mom-and-pop" outfitters.

**Baking in Costs**

Robinson told the *Journal* that larger companies, haven't explicitly tacked on surcharges, but expects that as contracts end, bigger vendors will seek to "bake it in to the contract renewals." Companies trying to pass on the cost of the tax would feel "a very swift and vocal objection in the marketplace," said Pete Allen, senior vice president of sourcing operations at the hospital-owned group-purchasing organization Novation.

"While most device manufacturers are taking responsibility for this tax, there are some manufacturers attempting to pass their obligation on to hospitals," Novation President and CEO Jody Hatcher said in prepared remarks. "This tax should be the responsibility of the manufacturers, and Novation is dedicated to ensuring that member hospitals are impacted by it as little as possible."

*—WE (February 4, 2013)*

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